REMARKS

I. Status of the claims

Claims 4, 11, 12, 34, 37, 38, 41 - 47 are pending. Claim 12 remains withdrawn. Claims 11, 37 and 41 have been amended to cancel the hepatitis B virus (HBV) in favor of the hepatitis C virus (HCV). New claims 42 – 47 have been added. The new claims are parallel to claims 4, 11, 34, 37, 38 and 41, but refer to the hepatitis B virus (HBV) rather than the hepatitis C virus (HCV). No new matter has been entered.

At the outset, even though the amendment is filed in response to a final rejection, this amendment is filed with a RCE, and therefore a showing under 37 CFR 1.116 is not required at this time.

II. Summary of the Interview with the Examiner

Applicants are grateful to the Examiner for his time on November 8, 2006 to discuss the above-referenced application. During the interview, the Examiner mentioned that the claims as they stood were too broad, and could not be practiced without undue experimentation. He noted during the interview, as he did in the Office Action, that the claims were enabled for a method for detecting HCV virus with the limitations recited at page 3, lines 1-5 of the Office Action. Applicants also discussed the Declaration and specifically the SDS value, and explained to the Examiner that there was a misunderstanding. The Examiner commented that in view of the Declaration, it was unclear whether the initial or final concentrations were recited. No agreement was reached during the interview.

III. Rejection of claims under 35 USC 112

The rejection of claims 4, 11, 34, 37, 38, 41, under 35 USC 112, first paragraph for lack of enablement is respectfully traversed.

The Examiner repeated his argument by referring to page 48 of the specification which gives an example of the reaction buffer as consisting of 100mM sodium phosphate buffer, ph 7.3, containing 0.15MNaCl, 1% BSA, 0.5% Casein-Na,

0.05% Tween 20 and 1M Tris. The Examiner alleges that the reaction buffer should be limited to this example and an example of the treatment solution as consisting of guanidine hydrochloride, HCL, Triton X 100 and Tween 20 does not reasonably provide enablement for methods of detecting HCV utilizing treatment solutions or reaction buffers other than those as set forth on page 48 and does not enable any methods for detecting HBV.

In this regard, the claims 11, 37 and 41 have been amended to cancel reference to the hepatitis B virus (HBV), the virus which is allegedly not enabled according to the Examiner. The hepatitis B virus (HBV) has been recast in new claims 42- 47, which parallel claims 4, 11, 34, 37, 38, and 41. Regarding the Examiner's position for lack of enablement, Applicants makes the following comments:

As indicated above during the interview, Applicants mentioned to the Examiner that there was a misunderstanding as to the recited SDS value in the Declaration. Applicants believe there is no inconsistency between the recited value of 1.25% SDS and the 5% value recited in the specification. As explained during the interview, the 1.25% value in the Declaration is the concentration of SDS when it's diluted from 5%. Therefore, Applicants do not believe these values are inconsistent. However, should the Examiner require a new Declaration, Applicants will do so.

On page 4, lines 17 to 21 of the Office Action, the Examiner stated that "The specification gives no guidance as to what combination of components, other than those set forth above, would result in a treatment solution that would inactivate the endogenous antibodies present in the biological sample (step 1 of the claimed methods) but not inactivate the antibody probe subsequently used the immunoassay (step 2 of the claimed methods)."

However, Applicants respectfully point out that the specification, on page 21, lines 20 to 34, describes that "the addition of a treatment agent containing a surfactant other than an anionic surfactant such as SDS can weaken the denaturing effect of SDS on the immobilized antibody and, as a result, can enhance sensitivity as compared to the addition of a treatment agent containing SDS alone."

In addition, as an example of "a treatment agent containing a surfactant other than an anionic surfactant such as SDS can weaken the denaturing effect of SOS on the immobilized antibody", Example 4 exhibits the effects of "amphoteric surfactant" exemplified by CHAPS, "protein denaturant" exemplified by Urea, and of "nonionic surfactant" exemplified by Triton X-100. In Example 4, after the sample was treated, "l6O μL of a reaction buffer and 80 μL of the treated sample were added to a well in which antibodies C11-3 and C11-7 were immobilized." The ratio of the reaction buffer and the treated sample is different from that in Example 5.

However, in the Declaration submitted previously, Applicants points out that a conventional reaction buffer can be used in the present invention. Therefore, a multitude of reaction buffers is not contemplated as the Examiner alleged at page 4, line 10 of the Office Action. Applicants would remind the Examiner that "the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." MPEP 2164.01.

In addition, "Enzyme Immunoassay of Immunoreactive Progastrin-Releasing Peptide (31-98) as Tumor Marker for Small-Cell Lung Carcinoma: Development and Evaluation" (Aoyagi, K. et al., Clin. Chem. 41/4, p537—543, 1995), which is submitted herewith, describes a method of measurement of Progastrin-Releasing Peptide (Pr0GRP) by ELISA. In this article, the section "Competitive-binding ELISA" on page 539 refers to "assay buffer (10 gIL BSA, 0.5 mL/L Tween 20, and 0.15 mol/L NaCl, in 0.1 mol/L phosphate buffer, ph 7.3)", and the section "Sandwich ELISA for ProGRP (31—98)" refers to "Reaction buffer (10 gIL BSA, 20 mmol/L EDTA, 0.5 mol/L NaCl and 0.5 mL/L Tween 20 in 0.1 mol/L phosphate buffer, ph 7.3)". The reaction buffer used in the Declaration is a minor modification of this buffer. Again, Applicants emphasize that if experimentation is necessary, which is not conceded here, it is not undue.

On page 5, lines 5 to 11 of the Office Action the Examiner stated that "While the skill in the art of immunology, chemistry and protein chemistry is high, one of skill in the art would not be able to contemplate what combination of treatment solution

components, reagent buffer components and antibody probe (other than those set forth above) would meet the limitations of the claimed methods since the antibody probe (which must remain functional in order to be used to detect viral antigens in the immunoassay) and the endogenous antibodies (which must be inactivated) are exposed to the identical conditions."

In response to the Examiner's view, the Applicants refer to the content of a biochemical textbook, regarding binding of SDS and proteins. It is well known that about 1.4 g of SDS which is a strong modifier of proteins bonds to 1 g of proteins (New Biochemical Experimental Manuals, Proteins I, page 356; printout of a web page from Sigma-Aldrich teaching Product No. L3771, which is submitted herewith). Since protein concentration in serum is 50 to 100 mg/ml, in the event where 5% SDS (50 mg/ml) and the same volume of serum are mixed, there is a high probability that most of SDS binds to proteins in the serum. After the treatment, therefore, at the time of reaction between a sample and an antibody probe, Applicants submit that an amount of residual SDS is not enough to strongly denature an antibody probe. Moreover, Applicants point out that after the treatment, the sample is diluted with the reaction buffer, and a concentration of substance which denatures proteins in the treatment solution is decreased. Accordingly it is believed that such a substance does not affect the reaction of the antibody probe and core antigen. Therefore, it is submitted that the above facts are well known in the art, and a person with ordinary skill in the art can easily work the claimed method in accordance with the disclosure in the specification.

Regarding the Applicants' argument 3, the Examiner stated in the Office Action, on page 5, line 20 to page 6, line 2, that "It should be noted that the concentrations of solution components in HBV and HCV solutions differ, Moreover, the specification discloses no examples detecting HBV utilizing the combination of a "treatment solution" and a "reaction buffer". The only Example drawn to HBV utilizes a "treatment solution" only."

However, Applicants would refer the Examiner to the specification, on page 9, lines 10 to 20, which recites:

> Furthermore, HCV which is an RNA virus, and HBV which is a DNA virus, are viruses which form virus particles having a structure comprising a structural protein encapsulating genomic RNA or DNA and a membrane surrounding it. In either embodiment, by using a treating method of the present invention, there is provided detection or determination of virus characterized by disrupting a virus particle of not only HCV or HBV but also a virus having similar a structure thereto, by fully exposing the virus antigen, and by detecting or determining said antigen.

More specifically, Example 14 in the specification describes a method for measurement of HBV core antigen.

Furthermore, Applicants turn the Examiner's attention to the specification, on page 53, lines 2 to 4, which recites "After allowing to stand at room temperature for 2 hours, the 1% BSA solution was aspirated off, and 2O0~iL of the reaction solution was added." The specification, on page 53, lines 12 to 14 continues by disclosing "After the treatment, 50 µL thereof was added to a well filled with the reaction solution, and was incubated at room temperature for 90 minutes." This reaction solution is a conventional buffer as in the Examples relating to HCV in the specification and in Table A in the submitted Declaration. Accordingly, a person skilled in the art would know how to use the claimed method without undue experimentation regarding HBV.

For all of the above reasons, claims 4, 11, 34, 37, 38, 41 - 47 are clearly enabled and therefore are patentable.

Reconsideration and allowance of claims 4, 11, 34, 37, 38, 41 - 47 is respectfully solicited.

CONCLUSION

In view of the foregoing amendment to the claims and remarks, it is respectfully submitted that the instant invention as defined in claims 4, 11, 34, 37, 38, 41 - 47 is in full compliance with all the statutory requirements of Title 35 USC, and, therefore, it is earnestly requested that the Examiner's rejection be withdrawn and that the pending claims be passed to issue.

Respectfully submitted
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Enclosures:

- "Enzyme Immunoassay of Immunoreactive Progastrin-Releasing Peptide (31-98) as Tumor Marker for Small-Cell Lung Carcinoma: Development and Evaluation" (Aoyagi, K. et al., Clin. Chem. 41/4, p537—543, 1995)
- Printout of a web page from Sigma-Aldrich teaching Product No. L3771

CERTIFICATE OF MAILING

I hereby certify that this *Amendment* is being deposited with the United States Postal Service via First Class Mail addressed to Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on November 10, 2006.

M. McGarry (Typed or printed name of person mailing paper or fee)

_____ (Signature of person mailing paper or fee)